Message

From: Shams, Dahnish [Shams.Dahnish@epa.gov]
Sent: 7/14/2020 2:20:56 PM
To: Vandenberg, John [Vandenberg.John@epa.gov]; Soto, Vicki [Soto.Vicki@epa.gov]; Thayer, Kris [thayer.kris@epa.gov]; Kapraun, Dustin [Kapraun.Dustin@epa.gov]
Subject: RE: Ramboll's final comments on EPA Peer Review Materials - final Denka materials
Attachments: Background for Peer Review of Chloroprene PBPK Modeling_071420 FINAL.pdf; Chloroprene_uncertainty_analyses_071420 FINAL.pdf; Draft Charge Questions for Peer Review of Chloroprene PBPK Modeling_071420 FINAL.pdf

Received! I've pulled together what I think are the final versions. I did not see any changes in the uncertainty analyses from late June. Is that correct? There were changes in the background document and the charge questions.

- Dahnish

Chemical and Pollutant Assessment Division (CPAD)
Center for Public Health and Environmental Assessment (CPHEA)
Office of Research and Development, U.S. EPA
O: (202) 564-2758

From: Vandenberg, John <Vandenberg.John@epa.gov>
Sent: Tuesday, July 14, 2020 10:06 AM
To: Shams, Dahnish <Shams.Dahnish@epa.gov>; Soto, Vicki <Soto.Vicki@epa.gov>; Thayer, Kris <thayer.kris@epa.gov>; Kapraun, Dustin <Kapraun.Dustin@epa.gov>
Subject: FW: Ramboll's final comments on EPA Peer Review Materials - final Denka materials

These are the files sent to Denka. They're final - need to delete comments and accept all changes and make 508. We did not send EPA uncertainty analysis - I think current version is on Sharepoint.

From: Vandenberg, John
Sent: Thursday, July 09, 2020 10:21 PM
To: Walsh, Patrick <patrick-walsh@denka-pe.com>
Cc: Orme-Zavaleta, Jennifer <Orme-Zavaleta.Jennifer@epa.gov>; Cascio, Wayne <Cascio.Wayne@epa.gov>; Dunlap, David <dunlap.david@epa.gov>; Thayer, Kris <thayer.kris@epa.gov>
Subject: RE: Ramboll's final comments on EPA Peer Review Materials

Patrick,

We have reviewed the final comments (dated July 8 2020) from Denka/Ramboll on the draft Charge and Background documents and have attached what we expect are the final versions of these documents. We now will move forward to have the documents cleaned up (e.g., removing comments) and prepared for web availability (508 compliant versions). We also are reviewing the comments you provided on the EPA uncertainty analysis and will be making some revisions; this document also will be prepared for web availability. Thank you for providing these comments.

When we are informed of the date I will let you know of the anticipated publication of the Federal Register Notice announcing the peer review.

Once the contractor evaluates public comments on the candidate peer reviewers they will select the expert peer review panel and make arrangements for a virtual public meeting.

As agreed to during our February meeting, we will work with you (and through you with the Ramboll scientists) to prepare a presentation on the peer review materials for the public meeting. We are looking forward to creating an informative and effective presentation.

Please let me know if you have any questions.
Thanks,

John

From: Walsh, Patrick <patrick-walsh@denka-pe.com>
Sent: Wednesday, July 08, 2020 6:49 PM
To: Vandenberg, John <Vandenberg.John@epa.gov>
Cc: Orme-Zavaleta, Jennifer <Orme-Zavaleta.Jennifer@epa.gov>; Cascio, Wayne <Cascio.Wayne@epa.gov>; Dunlap, David <dunlap.david@epa.gov>; Thayer, Kris <thayer.kris@epa.gov>
Subject: Ramboll's final comments on EPA Peer Review Materials
Importance: High

John,

Hope you had a restful weekend and holiday!

Before I forget, I still haven't seen the FRN yet. Do you have any idea when it will be published?

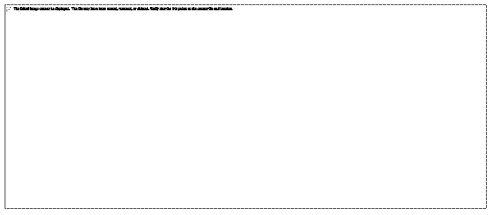
As for the documentation, I'm including Ramboll's comments on the background, charge, and uncertainty analysis documents. Notice that, for convenience, we broke out the few new comments into a cleaner document so they'll be easier to follow. The idea is that we think most of our remaining concerns can be settled during the peer review process, and we would like to get there sooner rather than later, given the fact that we first looked at peer review documents from EPA more than 9 months ago.

To that end, we appreciate EPA's consideration of our comments to date on the materials for the peer review of the Ramboll (2020) model. We have a few remaining comments for EPA to consider as part of the peer review materials; however, we don't want any further delays in initiating the peer review process. We ask that finalizing these materials be a priority so that the Ramboll (2020) model can move into peer review as soon as possible. Our remaining comments are limited to:

- In the Background Document:
  - We had added some language to clarify the introduction of a new dose metric (tissue concentration of the parent chemical) that is not part of the Ramboll (2020) report and is under consideration by EPA. While we have not modified the text, we do provide comments for consideration related to the science surrounding the proposed use of tissue concentration as a dose metric for the cancer risk assessment, i.e., that the science does not support using tissue concentration as a dose metric because it is inconsistent with the accepted mode of action.
- In the Charge Questions Document:
  - We appreciate the input on the tiered process and agree with most of the suggested edits. However, there is still confusion over the use of the Wood et al. (2017) paper as a way to evaluate the ability of IVIVE to be used for chloroprene. We have suggested additional edits to clearly point out that the Wood et al. (2017) paper focuses on oral dosing of drugs, not inhalation of volatile compounds, such as chloroprene. It is probably most appropriate to remove reference to the Wood paper entirely as a result.
- In the Uncertainty Analysis Document:
  - We recognize that EPA is not requesting comments on this document; however, we think it is important to convey anything we have identified that could be an incorrect assumption and impact the results of the analysis. In particular, we have noted some aspects of the MCMC approach that we believe are less than optimal and could result in failure to obtain convergence for the parameter estimates. We would be happy to continue the dialog with the EPA scientists performing the analysis to optimize the likelihood of success.

- We also have significant concerns surrounding this new, complex uncertainty analysis of the human lung tissue metabolism data in order to estimate an alternative value. Because these data are highly uncertain, any resulting estimates from this complex analysis would not provide a reliable alternative to the estimates obtained using currently accepted approaches.

Again, we appreciate the opportunity to work with EPA to finalize these materials for the peer review. Please let us know at your earliest convenience whether there are any remaining questions or if these materials are ready to be finalized.



Patrick A. Walsh, CIH | SHE Manager
Denka Performance Elastomer LLC
560 Highway 44 | LaPlace, LA 70068
Office: 985-536-7573 | Cell: 251-321-5989
patrick-walsh@denka-pe.com